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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **IMPROVED rAAV VECTORS**

(57) Abstract: Disclosed are methods for use of therapeutic polypeptide-encoding polynucleotides in the creation of transformed host cells and transgenic animals. In particular, the use of recombinant adeno-associated viral (rAAV) vector compositions that specifically target mammalian cells, such as pancreatic islets cells, that express low-density lipoprotein receptors on their cell surface. The disclosed vectors comprise one or more polynucleotide sequences that express one or more mammalian polypeptides having therapeutic efficacy in the amelioration, treatment and/or prevention of AAT- or cytokine polypeptide deficiencies, such as for example in diabetes and related diseases, as well as a variety of autoimmune disorders including, for example, lupus and rheumatoid arthritis.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/12225

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/864, 7/00, 7/01, 5/10; A61K 48/00

US CL : 435/320.1, 325, 366, 69.1, 455, 456, 457; 424/93.1, 93.2, 93.6

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/320.1, 325, 366, 69.1, 455, 456, 457; 424/93.1, 93.2, 93.6

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YANG et al. Development of Novel Cell Surface CD34-Targeted Recombinant Adenoassociated Virus Vectors for Gene Therapy. Human Gene Therapy. 01 September 1998, Vol. 9, pages 1929-1937, especially Fig. 1 and pages 1933-1934.	1-3, 8-10, 14-34 and 44-51
A	US 5,863,541 A (SAMULSKI et al.) 26 January 1999 (26.01.1999), columns 2-3.	1-3, 8-10, 14-34 and 44-51
A	US 6,261,834 B1(SRIVASTAVA) 17 July 2001 (17.07.2001), column 3, lines 34-63.	1-3, 8-10, 14-34 and 44-51
A,P	BOWLES et al. Marker Rescue of Adeno-Associated Virus (AAV) Capsid Mutants: a Novel Approach for Chimeric AAV Production. Journal of Virology. January 2003, Vol. 77, No. 1, pages 423-432, especially Figures 1 and 6 and pages 425 and 427.	1-3, 8-10, 14-34 and 44-51



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

08 September 2003 (08.09.2003)

Date of mailing of the international search report

02 JUN 2004

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/12225

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claim Nos.: 4-7 and 11-13
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
The claims read on SEQ ID NOs but are unsearchable because a computer readable form of the Sequence Listing was not supplied.
3. ☒ Claim Nos.: 35-43
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.